

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

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Serial No.: To be assigned Group Art Unit: To be assigned

Filed: Concurrently herewith Examiner: To be assigned

For: PESTIVIRUS MUTANTS AND VACCINES CONTAINING THE SAME

Corresponding to: EP 00201 421.5, filed April 21, 2001

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

April 20, 2001

Sir:

Prior to the examination of the above-referenced application, please amend the same as follows.

IN THE CLAIMS:

Please cancel claims 1-14 without prejudice or disclaimer of the subject matter thereof and add new claims 15-47.

15. An attenuated pestivirus mutant having a reduced ability to replicate relative to a wild-type pestivirus, said mutant comprising one or more mutations of one or both of stem loops Ia and Ib of the 5' nontranslated region (NTR) of the pestivirus genome, and wherein the 5' end of the genome comprises the nucleotide sequence 5'-GUAU and expression of a viral polyprotein is under the control of a homologous internal ribosome entry site (IRES).

16. The pestivirus mutant of claim 15, wherein said reduced ability to replicate is exhibited by a small plaque size phenotype.

17. The pestivirus mutant of claim 15, wherein the mutant comprises more than one mutation in one or both of the stem loops Ia and Ib.

18. The pestivirus mutant of claim 15, wherein the one or more mutations is a deletion of one or more nucleotides.

19. The pestivirus mutant of claim 15, wherein the one or more mutations is a deletion of stem loop Ia, or a part thereof.

20. The pestivirus mutant of claim 15, wherein the one or more mutations is a deletion of stem loop Ia and part of stem loop Ib.

21. The pestivirus mutant of claim 15, wherein the one or more mutations is a deletion of stem loops Ia and Ib, and wherein the nucleotide sequence at the 5' end of the genome is 5'-GUAUUAU or 5'-GUAUCCU.

22. The pestivirus mutant of claim 15, wherein the loop portion of stem loop Ib, if present, contains five adenosine (A) residues.

23. The pestivirus mutant of claim 15, wherein the pestivirus is bovine viral diarrhea virus (BVDV).

24. The pestivirus mutant of claim 23, wherein the pestivirus is BVDV-1 or BVDV-2.

25. A method of attenuating a pestivirus by reducing the ability of the pestivirus to replicate in a host relative to a wild-type pestivirus, comprising the step of mutating one or both of stem loops Ia and Ib of the 5' nontranslated region (NTR) of the pestivirus genome, wherein the 5' end of the genome comprises the nucleotide sequence 5'-GUAU and expression of a viral polyprotein is under the control of a homologous internal ribosome entry site (IRES).

26. The method of claim 25, wherein said reduction in the ability to replicate is exhibited by a small plaque size phenotype.

27. The method of claim 25, wherein any one or both of the stem loops are mutated more than once.

28. The method of claim 25, wherein any one or both of the stem loops are mutated by a deletion of one or more nucleotides.

29. The method of claim 25, wherein stem loop Ia, or a part thereof, is deleted.

30. The method of claim 25, wherein stem loop Ia and part of stem loop Ib are mutated.

31. The method of claim 25, wherein stem loops Ia and Ib are deleted, and wherein the nucleotide sequence at the 5' end of the genome is 5'-GUAUUAU or 5'-GUAUCCU.

32. The method of claim 25, wherein the loop portion of stem loop Ib, if present, contains five adenosine (A) residues.

33. The method of claim 25, wherein the pestivirus is bovine viral diarrhea virus (BVDV).

34. The method of claim 33, wherein the pestivirus is BVDV-1 or BVDV-2.

35. A vaccine comprising an immunologically active pestivirus mutant of claim 15, and a pharmaceutically acceptable carrier or diluent.

36. The vaccine of claim 35, wherein the vaccine provides a therapeutic effect in animals having pestivirus infections.

37. The vaccine of claim 35, wherein the vaccine further comprises an adjuvant.

38. The vaccine of claim 35, wherein the vaccine is freeze-dried or frozen.

39. The vaccine according to claim 35, wherein the pestivirus mutant is a BVDV mutant and the vaccine further comprises an immunogen derived from one or more of bovine rotavirus, bovine respiratory syncytial virus, bovine herpesvirus type 1, bovine coronaviruses, parainfluenza type 3 virus, bovine paramyxovirus, foot and mouth disease virus, infectious bovine rhinotracheitis virus and *Pasteurella hemolytica*.

40. A vaccine comprising an immunogenically effective dosage of the pestivirus mutant of claim 15, and a pharmaceutically acceptable carrier and diluent.

41. The vaccine of claim 40, wherein the vaccine is prophylactic.

42. The vaccine of claim 40, wherein the vaccine further comprises an adjuvant.

43. The vaccine of claim 40, wherein the vaccine is freeze-dried or frozen.

44. The vaccine of claim 40, wherein the pestivirus mutant is a BVDV mutant and the vaccine further comprises an immunogen derived from one or more of bovine rotavirus, bovine respiratory syncytial virus, bovine herpesvirus type 1, bovine coronaviruses, parainfluenza type 3 virus, bovine paramyxovirus, foot and mouth disease virus, infectious bovine rhinotracheitis virus and *Pasteurella hemolytica*.

45. A method of inducing immunity to a pestivirus infection, comprising administering to an animal the vaccine of claim 40.

46. A method of inducing immunity to a pestivirus infection, comprising administering to an animal the vaccine of claim 42.

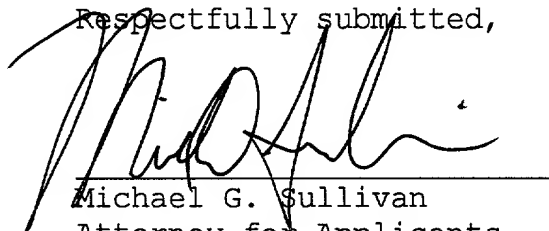
47. A method of making a vaccine for the protection or treatment of an animal against a pestivirus infection, comprising mixing together the pestivirus mutant of claim 15 and a pharmaceutically acceptable carrier.

REMARKS

Claims 1- 14 are cancelled and new claims 15-47 are presented for examination. These new claims are presented to conform the language of the claims to accepted U.S. patent practice, to eliminate multiple dependencies, to recite particular embodiments and to claim additional aspects of the invention disclosed in the specification without limiting the scope of the claims as first written and not for the reasons of patentability under 35 U.S.C.

It is believed that claims 15-47 recite a patentable improvement in the art. Favorable action is solicited. In the event any fees are required with this paper, please charge our Deposit Account No. 02-2334.

Respectfully submitted,



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